

Appl. No. 10/798,440
Amendment dated: January 14, 2005
Reply to OA of: September 17, 2004

REMARKS

The present amendment is in response to the Office Action mailed September 17, 2004, in which claims 1-22 were rejected. Applicant has thoroughly reviewed the outstanding Office Action including the Examiner's remarks and the references cited therein. The following remarks are believed to be fully responsive to the Office Action and, when coupled with the amendments made herein, are believed to render all claims at issue patentably distinguishable over the cited references.

In the specification, the 4th paragraph of page 2, 2nd paragraph of page 5, 2nd paragraph of page 7 and 1st paragraph of page 8 have been amended to correct the specification to overcome the objections to the specification. The generic expression for the Trademark, TALON has been provided as requested in the official Action. This amendment does not introduce new matter into the specification and claims as it simply provides information as would be known by one of ordinary skill in the art at the time the application was filed. Accordingly, it is most respectfully requested that the objection be withdrawn.

Claims 1, 2, 12, 19 and 22 are amended. No claims are added. Accordingly, claims 1-22 remain pending.

All of the amendments are fully supported by the original disclosure of this application and therefore do not constitute the introduction of any new matter into this application. The amendments to the claims clearly obviate the objection to the claims and therefore it is requested that the objection to the specification be withdrawn.

Applicant most respectfully submits that all the claims now present in the application are in full compliance with 35 U.S.C. §112 and are clearly patentable over the references of record.

Applicant respectfully requests reconsideration in light of the above amendments and the following remarks.

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CLAIM REJECTIONS - 35 USC §103 (a)

Claims 1-22 are rejected under 35 USC 103(a) as being anticipated by Enomoto et al. (Biotechniques (1998) 24:782-788) in view of Cosma (US 6,150,123) and Terpe (Appl. Microbiol biotechnol (2003) 60:523-533). Of the rejected claims, claim 1 is an independent claim. Applicant respectfully traverses this rejection. This rejection has been carefully considered but is most respectfully traversed.

Applicants wish to direct the Examiner's attention to the basic requirements of a *prima facie* case of obviousness as set forth in the MPEP § 2143. This section states that to establish a *prima facie* case of obviousness, three basic criteria first must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Section 2143.03 states that all claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence present by applicant and the citation of *In re Soni* for error in not considering evidence presented in the specification.

The amended claim 1 is drawn to a substrate, coated with recombinant protein, fabricated by a method comprising steps of purification, modification, and immobilization

of said recombinant protein. Enomoto teaches the expression of epitope- and affinity-tagged fusion proteins in yeast and *E. coli*. The affinity tag is composed of six consecutive histidine residues that enable the facile purification of a fusion protein on a metal column. However, Enomoto does not disclose the steps of biotinylation and immobilizing the fusion protein nor does this reference suggest this modification.

As to the present invention, see the page 3, line 15-20 and page 8, example 1 of the specification. The affinity column is not only used for the step of purifying the recombinant fusion protein but also for the step of biotinyling the recombinant fusion protein bound in the column. Comparing with Enomoto, the fusion protein will be eluted from the column directly without any modification after the undesired proteins flushed out. Accordingly, the tag with affinity to its binding partner disclosed in the present invention provides additional functions different from Enomoto.

Additionally, Cosma teaches a method for detectably labeling with biotin a subset of a larger population of proteins. However, the affinity biotinylation procedure is used for the detection of the target protein. The presence of the protein will be recognized by the intensity of the isotoped- or dyed- avidin binds to the biotinylated protein. Moreover, the target protein may only be recognized by corresponding ligand. Each protein needs its own column to be captured in when carrying the biotinyling process. The present invention fuses the specific tag onto the desired protein. It means that the corresponding column can capture a series of desired proteins containing the tag. Besides, the object of the biotinyling step in the present invention is used for protein immobilization but not purification. Accordingly, the purpose and effect of biotinylation step in the present invention are different from Cosma.

Moreover, Terpe teaches the importance of immobilization of biologically active proteins for research and industry. However, the meaning of the last three sentences in the conclusion should be drawn back to the importance of protein immobilization by the tag with affinity to its binding partner according to the first sentence "Many tags with high affinity to their binding partner are also useful tools to immobilize peptides or proteins on surface."(See page 530, column 2, line 15) and the last sentence

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"Furthermore, the importance of affinity-tag technology..."(See page 530, column 2, line 19). However, the limitation of fusion protein, "Sometimes the fused protein cannot be purified because the tag is not surface exposed" has also been disclosed (See Terpe p.530, Conclusion section, the sixth sentences). The solutions of the limitation, denaturing or placing the tag at the other terminus, often combine with the losing of the protein activity. The present invention uses the tag as a purifying and modified functional group but not for immobilization. Besides, the present invention uses the affinity between biotin and avidin for protein immobilization. Although it is well known in the art that biotin binds avidin, the purpose of using biotin is for detection or purification a target protein (e.g. a dyed- or isotoped avidin binding to a biotinylated protein or the affinity site of the ICAT reagent). While major purpose of utilizing the affinity of biotin and avidin in the present invention is for immobilizing a recombinant protein onto a substrate to fabricate an immobilized substrate for the subsequent applications. Accordingly, the purpose of the present invention is different from the Terpe. The necessary motivation to modify the prior art must be found in the references as combined. Applicants' specification may not be used as a teaching reference to combine the teachings and arrive at Applicants' claimed invention. *In re Fritch, 23 USPQ 1780, 1784(Fed Cir. 1992)* ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.).

Hence, the present invention discloses a method for fabricating a substrate by purification, modification, and immobilization of recombinant protein. It combines the advantage of prior arts to achieve a "one pot reaction" and every single step of the method is given an additional function or a new purpose different from the prior art. The combination will make cost down for fabricating the substrate with the recombinant protein by reducing the loss of the protein coated on the substrate and raising the purity of the protein.

For the reason discussed above, reconsideration and withdrawal of the Examiner's rejection under 35 USC §103 (a) is most respectfully requested.

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In view of the above comments and further amendments to the specification and claims, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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